REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 15-20 are pending in the present application. Claims 1-14 have been canceled. Support for claims 15-20 may be found in previously pending claims 1-14 and generally throughout the specification. In particular, support for new claims 15-20 may be found in the present specification at page 2, line 32 to page 3, line 5; page 3, lines 24-28; and page 4, lines 14-15.

Applicant also notes that the present specification has been amended to correct several informalities recently detected by the applicant. Page 4, line 6, the term "5 % air" has been deleted in favor of the term "95 % air". In view of Example 1 at page 7, line 11, applicant believes that it is apparent that the term should be "95 % air".

The term "GM, CSF" at page 4, line 35 has been amended to recite "GM-CSF". Applicant respectfully submits that it is evident to one of ordinary skill in the art that the term should be "GM-CSF" in view of Table 1.

In the specification at page 3, lines 7-8 and page 4, line 13, the term "the humanized biomaterial according to any of claims 1 to 3" has been deleted and the term "the humanized biomaterial as described above" has been inserted. As noted

above, claims 1-3 have been canceled. Thus, it was necessary to delete this recitation.

In the outstanding Official Action, claims 1-4 were rejected under 35 USC 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In imposing the rejection, the outstanding Official Action rejected claims 1-4 for reciting the terms "and preferably with macrophages", "such as aluminum oxide", "are liable to be", "for instance", and "preferably". However, as noted above, claims 1-4 have been canceled. Claims 15-20 have been drafted in a manner so that these terms no longer appear in the claims.

The outstanding Official Action further rejected claim 2 for alleging being indefinite for not reciting proper Markush language. Applicant believes that claims 15-20 recite proper Markush language.

The outstanding Official Action also objected to the term "patient's" in claim 3. The Official Action alleged that the term lacked antecedent basis. As noted above, claim 3 has been canceled. Applicant believes that the terms recited in claims 15-20 are all provided proper antecedent basis.

Claim 4 was rejected for reciting "comprises" and "consists of" in the same claim. The Official Action alleged that the claim was indefinite as it recited two different transitional phrases. As suggested by the Examiner, the claims have been drafted so that two transitional phrases are no longer recited in a single claim.

In view of the above, applicant believes that claims 15-20 are definite to one of ordinary skill in the art.

Claims 1-4 were rejected under 35 USC 102(b) as allegedly being anticipated by NAUGHTON et al. Claims 1-4 were then rejected under 35 USC 103(a) as allegedly being obvious in view of NAUGHTON et al. These rejections are respectfully traversed.

The claimed invention is directed to humanized biomaterial comprising a porous biocompatible material customized and implanted with monocyte-derived cells substantially irreversibly bound to said biomaterial. The expression "humanized" means that porous biomaterial has been colonized with human cells derived from blood monocytes (page 1, lines 32-33). The expression "monocyte-derived cells" corresponds to human mononuclear cells isolated from blood, enriched in monocytes and cultured at 37°C in appropriate medium for 5 to 10 days to obtain tissue type macrophages (page 2, lines 5-7 and lines 32-33; and page 7, example 1). Therefore, the cell suspension used to

humanize the biomaterial, and said humanized biomaterial, contains substantially only monocyte- derived cells or macrophages. The expression "substantially irreversibly bound" means that macrophages are tightly bound by numerous contacts with the material and cannot be detached under physiological conditions.

Applicant does not believe that NAUGHTON et al. disclose or suggest the claimed invention. NAUGHTON et al. disclose a three-dimensional cell culture system wherein cells derived from a desired tissue are inoculated and grown on a pre-established stromal support matrix (col. 2, lines 55-66). The stromal cells are fibroblasts, but may include other cells found in loose connective tissue such as macrophages and monocytes (col. 2, lines 55-66).

NAUGHTON et al. teach that the stromal cells are defined as being fibroblasts with or without (emphasis added) other cells and/or elements found in loose connective tissue (see U.S. 4,963,489, col. 3, lines 45-49). Consequently, the monocytes or macrophages may be optionally present in the three-dimensional cell culture system and when they are present they constitute only a very low proportion of the cells. Indeed, the fibroblasts are the predominating cells (col. 17, lines 36-37).

Therefore, the three-dimensional cell culture system described by NAUGHTON et al. does not substantially comprise monocyte-derived cells or macrophages.

Thus, NAUGHTON et al. disclose a three-dimensional cell culture system wherein the stromal support matrix comprises predominantly fibroblasts with optionally macrophages (col. 3, lines 45-49). This three-dimensional cell system may be used as implantable system once the appropriate cells have been grown (col. 3, lines 26-36).

However, the present invention is directed to implanting a porous biocompatible material comprising substantially only monocyte-derived cells, which bind substantially irreversibly to the biomaterial (page 1, lines 29-33; page 2, lines 5-10 and 32-37; and page 3, lines 1-5).

As a result, applicant believes that the disclosure of NAUGHTON et al. teaches away from the present invention. NAUGHTON et al. teach that the fibroblasts are used as support cells owing to their particular properties (col. 2, lines 67-69; col. 3, lines 164 and lines 45-49) that the macrophages are not deemed to possess, which means that they are not interchangeable with the fibroblasts.

Moreover, the preparation of the three-dimensional cell culture system relies upon the growth and the proliferation of the stromal cells, which are fibroblasts, in the mesh of the

matrix (col. 9, lines 18-38, col. 17, lines 36-39). However, it is well known by one skilled in the art that differentiated macrophages no longer proliferate.

In addition, it has been observed that when the three-dimensional cell culture system is used to grow bone marrow cells and various hematologic lineages, they bind only loosely on the matrix areas without support cells (i.e. predominantly fibroblasts). This indicates that without fibroblasts, the hematologic lineages (comprising macrophages) do not bind to the overall matrix (col. 28, lines 41-54), col. 31, lines 12-14).

As a result, NAUGHTON et al. do not provide the necessary motivation to one skilled in the art to modify the teaching of NAUGHTON et al. to obtain the claimed invention.

Claims 1-4 were rejected under 35 USC 102(e) as allegedly being anticipated by LEE et al. Claims 1-4 were also rejected under 35 USC 103(a) as allegedly being obvious in view of LEE et al. These rejections are respectfully traversed.

The LEE et al. publication is directed to a synthetic, poorly-crystalline apatitic (PCA) calcium phosphate material seeded with cells (see abstract). This material is porous (col. 9, lines 45-46) and may be seeded with macrophages (col. 10, lines 26-34). However, it is disclosed that the seeding of this material with macrophages is intended for purposes of *in vitro* studies (col. 10, lines 26-34). There is no mention in the

document that the PCA calcium phosphate material seeded with macrophages could be used for preparing humanized biomaterial.

Applicants do not believe that LEE et al. would have prompted one skilled in the art to modify the LEE et al. publication to obtain the claimed invention.

LEE et al. state that one of the essential features for scaffold material intended to be implanted *in vivo* is that neither the scaffold material nor its degradation products should provoke inflammation or toxicity when implanted *in vivo* (col. 1, lines 49-51). This corresponds to the biocompatibility of the scaffold material (col. 2, lines 20-31).

By contrast, one of the features of the present invention is an inflammation step induced by the macrophages which aids in inducing migration and homing of competent cells for tissue repair (page 8, lines 15-17).

As a result, the teaching of LEE et al. would have directed one of ordinary skill in the art away from the claimed invention.

Indeed, LEE et al. do not teach that macrophages may provide support for the growing of competent cells for tissue repair or may bind substantially irreversibly to the biomaterial.

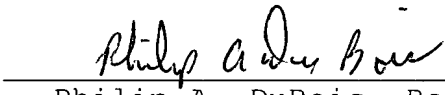
In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 15-20, as presented.

Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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